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# Lipoprotein ratios are better than conventional lipid parameters in predicting coronary heart disease in Chinese Han people

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## Abstract

**Background and aim:** Dyslipidaemia is the main risk factor for coronary heart disease (CHD). Plasma lipid levels are conventionally used to predict coronary risk globally, but further studies are required to investigate whether the lipoprotein ratios are superior to conventional lipid parameters as predictors for CHD.

**Methods:** A hospital-based case-control study consisting of 738 CHD patients and 157 control subjects was conducted in a Chinese Han population. Demographic characteristics and plasma lipid or apolipoprotein data were collected. Univariate and multivariate logistic regression analyses were carried out to examine the relationship between the lipoprotein ratios and CHD risk.

**Results:** The CHD group had significantly higher age, non-high-density lipoprotein cholesterol (non-HDL-C), lipoprotein (a) [Lp(a)], triglyceride (TG)/HDL-C, total cholesterol (TC)/HDL-C, low-density lipoprotein cholesterol (LDL-C)/HDL-C, non-HDL-C/HDL-C, very low-density lipoprotein cholesterol (VLDL-C)/HDL-C, and apolipoprotein B100/apolipoprotein AI (apoB100/apoAI) than the control group ($p < 0.05$ for all). Moreover, the prevalence of male sex, smoking, and hypertension in the CHD group was significantly higher than in the control group. The results from univariate logistic regression analysis showed that the ratios of TC/HDL-C (OR 1.135, 95% CI 1.019–1.265), LDL-C/HDL-C (OR 1.216, 95% CI 1.033–1.431), non-HDL-C/HDL-C (OR 1.135, 95% CI 1.019–1.265), and apoB100/apoAI (OR 1.966, 95% CI 1.013–3.817) significantly increased the risk for CHD. By multivariate logistic regression analysis, the results were not materially altered and each of the four ratios was independently associated with CHD after adjustment for non-lipid coronary risk factors. ApoB100/apoAI showed the strongest association with CHD in both the univariate and multivariate logistic regression analyses.

**Conclusions:** Our data indicate that the lipoprotein ratios are superior to conventional lipid parameters as predictors for CHD. Of the ratios, apoB100/apoAI is the best to predict CHD risk.

**Key words:** coronary heart disease, lipoprotein ratio, apoB100/apoAI, dyslipidaemia, predictor

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## INTRODUCTION

Coronary heart disease (CHD) is a leading cause of morbidity and mortality in developed countries and is rapidly assuming epidemic proportions in developing countries, including China. CHD is recognised as a multifactorial disease, and dyslipidaemia accounts for around 50% of the population-attributable risk [1]. Reliable indices for CHD risk assessment and targets for drug treatment are important to manage and prevent this disease. At the present time, increases in plasma total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), non-high-density lipoprotein cholesterol (non-HDL-C), very low-density lipoprotein cholesterol (VLDL-C), triglyceride (TG), and/or lipoprotein (a) [Lp(a)] and decreases in HDL-C are commonly used as CHD predictors in clinical practice.

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According to the Adult Treatment Panel III (ATP III) guidelines [2] and the 2013 American College of Cardiology/American Heart Association (ACC/AHA) blood cholesterol guidelines [3] of the United States, LDL-C was considered as the major cause of CHD and used as the primary target for therapy, and the other lipid parameters were used as secondary or supplementary targets.

However, there are more and more arguments among epidemiologists and clinicians that coronary risk assessment based exclusively on LDL-C is not optimal, particularly in individuals at intermediate risk [4–6]. Efforts have been made in seeking emergent or new cardiovascular risk markers to improve CHD prediction. Of great interest are the lipoprotein ratios that have atherogenic components (e.g. LDL-C) in the numerator and antiatherogenic components (e.g. HDL-C) in the denominator. The ratios can comprehensively reflect the balance between the atherogenic and antiatherogenic potentials in an individual. There is growing evidence that the HDL-C related ratios, including TC/HDL-C, LDL-C/HDL-C, non-HDL-C/HDL-C, VLDL-C/HDL-C, and TG/HDL-C, are superior to conventional lipid parameters as predictors for CHD [6–8]. These ratios can provide more information on risk that is difficult to quantify by routine analyses and could be a better mirror of the metabolic and clinical interactions between lipid fractions. An increase in TC, LDL-C, non-HDL-C, VLDL-C, or TG concentrations is an atherogenic lipid marker, whereas reduced HDL-C concentration is an antiatherogenic trait, which may also be correlated with numerous other risk factors, including the components of the metabolic syndrome. Therefore, the lipoprotein ratios are theoretically better than any of the individual lipid parameters for CHD prediction and could give us more information.

Recent data from interventional and observational studies suggest that the apolipoprotein B100/apolipoprotein AI (apoB100/apoAI) ratio may be another new and strong CHD marker that is even better than the HDL-C-related ratios in CHD risk assessment [9, 10]. Each particle of the atherogenic lipoproteins (LDL, VLDL, intermediary density lipoprotein [IDL], and Lp[a]) carries one apoB100 molecule, so the concentrations of plasma apoB100 can reflect the total of atherogenic potentials. In contrast, apoAI is a major component of antiatherogenic HDL; the plasma content of apoAI represents the total of antiatherogenic potentials. Thus, the apoB100/apoAI ratio is supposed to be an accurate and comprehensive CHD risk marker; the lower the ratio, the lower the CHD risk.

The present study had two objectives. The first was to determine whether the lipoprotein ratios were superior to any of the conventional lipid parameters (i.e. TC, LDL-C, HDL-C, non-HDL-C, VLDL-C, TG, and Lp[a]) in predicting CHD risk in a Chinese Han population. If so, the second objective was to determine which ratio had the best predictive power for CHD.

## METHODS

### *Study participants*

This project was designed as a hospital-based case-control study. A total of 895 consecutive unrelated adult patients who underwent coronary angiography for suspected CHD at the Affiliated Hospital of North Sichuan Medical College (Nanchong, China) were enrolled in the study between May 2011 and April 2014. Of these subjects, 738 patients were diagnosed with CHD, while the rest 157 subjects were considered as the control group. Patients taking lipid lowering drugs or drugs that might affect the glucose or lipid metabolism were excluded from the study. In order to enlarge the sample size, those who took drugs that were thought not to affect plasma lipid levels were still enrolled in this study. Patients with renal or hepatic dysfunction, active inflammatory disease, significant valvular disease, myocarditis, and malignant disease were also excluded from the study. All the subjects were Chinese Han people. The Han people are the largest ethnic group in East Asia, constituting approximately 92% of the population of Mainland China, 98% of the population of Taiwan, and 74% of the population of Singapore. The study protocol was approved by the ethics committee of North Sichuan Medical College. Written consent was provided by all the participants or their guardians prior to their participation in the study.

### *Coronary angiography and echocardiography*

Coronary angiograms were evaluated by experienced cardiologists who were unaware of the patients' biochemical status. Standard coronary angiography with at least four views of the left coronary system and two views of the right coronary artery were performed using the Judkins technique by Allura Xper FD20 (Philips Medical Systems Nederland B.V., Netherlands). CHD was diagnosed in patients who had angiographic evidence of stenosis greater than 50% in at least one major coronary artery. Those with normal coronary arteries or minimal stenosis (less than 50%) in any of the major coronary arteries were considered as control subjects. Each subject also underwent an echocardiographic evaluation using an iE33 ultrasound system (Philips Medical Systems, Best, Netherlands). Two-dimensional and M-mode echocardiographic evaluations were performed to measure the left ventricular end-diastolic diameter (LVEDD) and the left ventricular ejection fraction (LVEF).

### *Diagnostic criteria*

Body mass index (BMI) was calculated by dividing weight by height squared (kg/m$^2$). Smoking was defined as regular cigarette smoking. Hypertension was defined as the measurement of systolic/diastolic blood pressure higher than 140/90 mm Hg or active use of antihypertensive drugs. Diabetes mellitus was defined as fasting glucose levels above 126 mg/dL or active use of antidiabetic drugs or insulin.

### Biochemical measurement

Fasting blood samples were taken on the morning of the day before taking any lipid lowering drugs. Samples were immediately transported to the Department of the Clinical Laboratory of the Affiliated Hospital of North Sichuan Medical College for measurement of plasma lipids. TC, LDL-C, HDL-C, VLDL-C, and TG were measured directly by enzymatic methods. ApoB100, apoAI, and Lp(a) were measured by immunoturbidimetric assays. All the measurements were carried out using an automatic clinical chemistry analyser (Beckman Coulter AU5800, USA). Non-HDL-C was calculated by TC minus HDL-C. The lipoprotein ratios were also calculated.

### Statistical analysis

Data are presented as mean ± standard deviation (SD) unless otherwise stated. Continuous variables were tested for normality; if not, log transformation was applied. All statistical analyses were done using SPSS version 11.0, SPSS Inc., Chicago, IL, USA. The differences between the CHD patients and controls were calculated by $\chi^2$ test for categorical variables, and Student's t-test for continuous variables. Both univariate and multivariate logistic regression analyses were carried out to determine the association of variables with the prevalence of CHD. The results of logistic regression analysis are expressed as the odds ratio (OR) with 95% confidence intervals (95% CI). All p-values are two-tailed, and differences were considered significant if $p \leq 0.05$.

## RESULTS

### Anthropometric, echocardiographic, and biochemical characteristics of the CHD patients and control subjects

The anthropometric, echocardiographic, and biochemical characteristics of the CHD patients and control subjects are shown in Table 1. The mean age of CHD patients was higher than that of control subjects ($p < 0.001$). The prevalence of male sex, smoking, and hypertension was greater in CHD cases than control subjects ($p < 0.05$ for all). There were no significant differences in weight, BMI, prevalence of alcohol drinking and diabetes, and echocardiographic parameters (LVEDD and LVEF) between the two groups.

Patients with CHD had increased plasma levels of non-HDL-C ($p = 0.02$) and Lp(a) ($p = 0.024$). The CHD patients also had marginally insignificantly higher levels of LDL-C than the control subjects ($p = 0.051$). There were no significant differences in TG, TC, HDL-C, VLDL-C, apoAI, and apoB100 between the two groups.

Comparing with the control group, the CHD group experienced significant increases in almost all the ratio indices, including TG/HDL-C ($p = 0.008$), TC/HDL-C ($p = 0.001$), LDL-C/HDL-C ($p = 0.001$), non-HDL-C/HDL-C ($p = 0.001$), VLDL-C/HDL-C ($p = 0.004$), and apoB100/apoAI ($p = 0.018$).

### Univariate logistic regression analysis for the association between lipid parameters and their ratios and CHD

The univariate logistic regression analyses showed that the ratios of TC/HDL-C, LDL-C/HDL-C, non-HDL-C/HDL-C, and apoB100/apoAI significantly increased the risk for CHD, with the OR and 95% CI of 1.135 (1.019–1.265), 1.216 (1.033––1.431), 1.135 (1.019–1.265), and 1.966 (1.013–3.817), respectively (Table 2). No significant associations were found between the isolated lipid or apolipoprotein parameters and CHD risk in our study population. TG/HDL-C and VLDL-C/HDL-C were also not associated with CHD risk by univariate logistic regression analysis.

### Multivariate logistic regression analysis for the association between lipid parameters and their ratios and CHD

Table 3 shows the ORs and 95% CI for CHD as computed by multiple logistic regression analyses. Higher ratios of TC/HDL-C, LDL-C/HDL-C, non-HDL-C/HDL-C, and apoB100/apoAI were independently associated with CHD after adjustment for age, sex, weight, and BMI in model 1. These results were not appreciably attenuated with the inclusion of alcohol consumption, cigarette smoking, hypertension, and type 2 diabetes mellitus in subsequent model 2 and model 3, indicating that these variables did not act as mediators of the relationship between the lipoprotein ratios and CHD. The association of apoB100/ApoAI with CHD was stronger than other lipoprotein ratios.

## DISCUSSION

It has been shown in our study that LDL-C and other conventional lipid parameters are not the best predictors correlating with the presence of CHD symptoms. To our knowledge, our study is the first to show this in a Chinese Han population. According to univariate and multivariate logistic regression analyses, the apoB100/apoAI ratio appears to be the strongest ratio to correlate with CHD, followed by the LDL-C/HDL-C ratio, and then the TC/HDL-C and non-HDL-C/HDL-C ratios.

The apoB100/apoAI ratio appeared to be the strongest predictor for CHD with the highest ORs under different regression models in the present study (Table 3). In theory, the apoB100/apoAI ratio is a highly valuable index for detecting atherogenic risk. On one hand, each particle of the atherogenic lipoproteins, i.e. LDL, VLDL, IDL, and Lp(a), carries one molecule of apoB100, so the concentrations of plasma apoB100 reflect the total of atherogenic potentials. On the other hand, apoAI is the major protein component of antiatherogenic lipoprotein, i.e. HDL. The serum content of apoAI, represents the total of antiatherogenic potentials. Therefore, the apoB100/apoAI ratio could be a comprehensive and accurate CHD risk marker. In practice, there is currently

Table 1. Anthropometric, echocardiographic, and biochemical parameters for coronary heart disease (CHD) patients and control subjects

| | Control group (n = 157) | CHD group (n = 738) | P |
|---|---|---|---|
| **Anthropometric parameters** | | | |
| Age [years] | 59.29 ± 9.21 | 63.23 ± 10.39 | < 0.001 |
| Weight [kg] | 62.45 ± 10.35 | 64.37 ± 9.71 | 0.062 |
| Body mass index [kg/m$^2$] | 24.04 ± 3.32 | 24.34 ± 2.98 | 0.351 |
| Male | 83 (52.87%) | 527 (71.41%) | 0.041 |
| Smokers | 53 (33.76%) | 449 (60.84%) | <0.001 |
| Drinkers | 38 (24.20%) | 217 (29.40%) | 0.322 |
| Hypertension | 47 (29.94%) | 353 (47.83%) | 0.008 |
| Diabetes mellitus (type 2) | 14 (8.92%) | 107 (14.50%) | 0.099 |
| **Echocardiographic parameters** | | | |
| LVEDD [mm] | 49.52 ± 8.76 | 48.25 ± 5.93 | 0.129 |
| LVEF [%] | 60.50 ± 11.98 | 61.39 ± 10.15 | 0.394 |
| **Lipid parameters** | | | |
| TG [mmol/L] | 1.44 ± 0.79 | 1.58 ± 1.08 | 0.114 |
| TC [mmol/L] | 4.04 ± 0.86 | 4.17 ± 1.05 | 0.139 |
| LDL-C [mmol/L] | 2.24 ± 0.60 | 2.35 ± 0.82 | 0.051 |
| HDL-C [mmol/L] | 1.03 ± 0.34 | 0.99 ± 0.32 | 0.201 |
| Non-HDL-C [mmol/L] | 3.01 ± 0.76 | 3.18 ± 1.06 | 0.020 |
| VLDL-C [mmol/L] | 0.76 ± 0.42 | 0.83 ± 0.56 | 0.161 |
| ApoAI [g/L] | 1.03 ± 0.22 | 1.00 ± 0.20 | 0.066 |
| ApoB100 [g/L] | 0.73 ± 0.21 | 0.75 ± 0.25 | 0.180 |
| Lp(a) [mg/L] | 265.54 ± 280.37 | 324.37 ± 351.97 | 0.024 |
| **Lipoprotein ratios** | | | |
| TG/HDL-C | 1.64 ± 1.43 | 2.08 ± 3.24 | 0.008 |
| TC/HDL-C | 4.22 ± 1.35 | 4.75 ± 3.07 | 0.001 |
| LDL-C/HDL-C | 2.37 ± 0.87 | 2.67 ± 1.70 | 0.001 |
| Non-HDL-C/HDL-C | 3.22 ± 1.35 | 3.75 ± 3.07 | 0.001 |
| VLDL-C/HDL-C | 0.85 ± 0.69 | 1.09 ± 1.66 | 0.004 |
| ApoB100/apoAI | 0.72 ± 0.23 | 0.78 ± 0.30 | 0.018 |

The differences between the CHD patients and controls were calculated by $\chi^2$ test for categorical variables, and Student's t-test for continuous variables; LVEDD — left ventricular end-diastolic diameter; LVEF — left ventricular ejection fraction; TG — triglyceride; TC — total cholesterol; LDL-C — low-density lipoprotein cholesterol; HDL-C — high-density lipoprotein cholesterol; VLDL-C — very low-density lipoprotein cholesterol; apoB100 — apolipoprotein B100; apoAI — apolipoprotein AI; Lp(a) — lipoprotein(a)

sufficient evidence to demonstrate that the apoB100/apoAI ratio is better for estimating cardiovascular risk than the conventional lipid parameters or the HDL-C related ratios. In a recent case-control study in Kathmandu Valley, Nepal, Tamang et al. [11] found that only the apoB100/apoAI ratio, HDL-C, and apoB100 were significantly associated with CHD; other lipid parameters and lipoprotein ratios were not found to be significant. Walldius et al. [12] found that the apoB100/apoA-I ratio was superior to any of the HDL-C related ratios for estimation of the CHD risk in 69,030 men and 57,168 women above 40 years of age after a mean follow-up of eight years. Another recent case-control study demonstrated that the combination of apoB100/apoA1 and non-HDL-C had an even greater predictive value than its individual components or other lipid parameters [13]. In the estimation of CHD risk, the apoB100/apoAI ratio was also found to have less error (underestimated or overestimated risk) than the conventional cholesterol ratios [14].

Individuals with a higher ratio of TC/HDL-C, LDL-C/HDL-C, or non-HDL-C/HDL-C had greater cardiovascular risk owing to the imbalance between the cholesterol molecules carried by atherogenic lipoproteins and those carried by antiatherogenic lipoproteins. This may be due to an increase in the atherogenic constituents contained in the numerator, or a decrease in the

antiatherogenic constituents of the denominator, or both. The TC/HDL-C ratio, but not the isolated TC or HDL-C, was found to be significantly associated with CHD in the present study (Table 2). The TC/HDL-C ratio was also shown to be an independent risk factor for CHD after adjustment for other non-lipid risk factors (Table 3). Our findings were consistent with the results of a prospective study in which Kinosian et al. [5] demonstrated that the TC/HDL-C ratio was a superior measure of risk for CHD compared with either TC or LDL-C levels. The TC/HDL-C ratio was found to be correlated with the severity of coronary lesions. In Chinese Han people, the severity of coronary lesions (according to the Gensini score of inpatients) was increased with the elevation of the TC/HDL-C ratio, but not the TG/HDL-C ratio [15]. As the TC/HDL-C ratio was considered a more sensitive and specific index of cardiovascular risk than TC, the Canadian working group have chosen this lipid ratio as a secondary goal of therapy [16]. However, American ATP III guidelines and the 2013 ACC/AHA blood cholesterol guidelines did not define the TC/HDL-C ratio as the primary target of therapy; nor is this ratio recommended as a secondary target of therapy [2, 3].

Table 2. Univariate logistic regression analyses for lipid parameters and their ratios with coronary heart disease (CHD) risk

| | Odds ratio | 95% CI | P |
|---|---|---|---|
| Lipid parameters | | | |
| TG [mmol/L] | 1.171 | 0.958–1.432 | 0.124 |
| TC [mmol/L] | 1.139 | 0.953–1.361 | 0.153 |
| LDL-C [mmol/L] | 1.210 | 0.957–1.529 | 0.111 |
| HDL-C [mmol/L] | 0.706 | 0.421–1.183 | 0.186 |
| Non-HDL-C [mmol/L] | 1.193 | 0.992–1.436 | 0.061 |
| VLDL-C [mmol/L] | 1.278 | 0.896–1.825 | 0.176 |
| ApoAI [g/L] | 0.465 | 0.204–1.060 | 0.068 |
| ApoB100 [g/L] | 1.565 | 0.752–3.255 | 0.231 |
| Lp(a) [mg/L] | 1.001 | 1.000–1.001 | 0.052 |
| Lipoprotein ratios | | | |
| TG/HDL-C | 1.101 | 0.984–1.232 | 0.092 |
| TC/HDL-C | 1.135 | 1.019–1.265 | 0.021 |
| LDL-C/HDL-C | 1.216 | 1.033–1.431 | 0.018 |
| Non-HDL-C/HDL-C | 1.135 | 1.019–1.265 | 0.021 |
| VLDL-C/HDL-C | 1.278 | 0.975–1.512 | 0.176 |
| ApoB100/apoAI | 1.966 | 1.013–3.817 | 0.046 |

The associations between the variables and CHD were analysed by univariate logistic regression; 95% CI — 95% confidence interval; other abbreviations as in Table 1

The LDL-C/HDL-C ratio appears to be as useful as the TC/HDL-C ratio. The results from our study show that the LDL-C/HDL-C ratio had a slightly higher predictive power for CHD as compared with the TC/HDL-C ratio (Table 3). Their similarity can be explained by the fact that approximately 70% of plasma TC is present in LDL-C and, consequently, TC and LDL-C are closely related regarding their predictive power for CHD risk. The LDL-C/HDL-C ratio may have more predictive power for CHD if hypertriglyceridaemia is taken into account. The subjects with combined high levels of LDL-C/HDL-C and TG had nearly four-times higher CHD risk compared with those without [17].

Non-HDL-C, which is the difference between TC and HDL-C, is a measure of all the cholesterol contained in atherogenic lipoproteins, such as VLDL, IDL, LDL, and Lp(a). Non-HDL-C has been recommended as a secondary therapeutic target in individuals with high TG concentration, and it has been suggested that it could be a surrogate marker of plasma apoB100 concentration in clinical practice. Unlike TG, non-HDL-C is not subject to wide intra-individual variations or the effects of incomplete fasting and, thus, may be a more convenient screening tool [18]. However, non-HDL-C is not always strongly associated with apoB100, particularly in the presence of hypertriglyceridaemia [19]. Although few studies have evaluated the non-HDL-C/HDL-C ratio for predicting CHD, it is assumed to have similar effects as those of the TC/HDL-C and LDL-C/HDL-C ratios [20].

The TG/HDL-C ratio was not associated with CHD in our study. The TG/HDL-C ratio was originally proposed by Gaziano et al. [21] as an atherogenic index that was proven to be a highly significant independent predictor for CHD, even stronger than TC/HDL-C and LDL-C/HDL-C. The ratio

Table 3. Multivariate logistic regression analyses for the lipoprotein ratios with coronary heart disease (CHD) risk

| Variable | Model 1[a] | | Model 2[b] | | Model 3[c] | |
|---|---|---|---|---|---|---|
| | Adjusted OR (95% CI) | P | Adjusted OR (95% CI) | P | Adjusted OR (95% CI) | P |
| TC/HDL-C | 1.166 (1.022–1.330) | 0.023 | 1.160 (1.017–1.323) | 0.027 | 1.169 (1.021–1.338) | 0.023 |
| LDL-C/HDL-C | 1.285 (1.047–1.576) | 0.016 | 1.273 (1.037–1.562) | 0.021 | 1.293 (1.047–1.596) | 0.017 |
| Non-HDL-C/HDL-C | 1.166 (1.022–1.330) | 0.023 | 1.159 (1.016–1.321) | 0.028 | 1.167 (1.020–1.336) | 0.025 |
| ApoB100/apoAI | 3.087 (1.249–7.630) | 0.021 | 2.910 (1.172–7.228) | 0.027 | 2.840 (1.143–7.056) | 0.025 |

The associations between the variables and CHD were analysed by multivariate logistic regression; [a]Model 1 — adjusted for age, sex, weight, and body mass index; [b]Model 2 — adjusted for variables in Model 1 plus alcohol consumption and cigarette smoking; [c]Model 3 — adjusted for variables in Model 2 plus hypertension and type 2 diabetes mellitus; OR — odds ratio; 95% CI — 95% confidence interval; other abbreviations as in Table 1

of TG/HDL-C was reported to be inversely correlated with the plasma level of small, dense LDL particles (sdLDL). As one component of atherogenic dyslipidaemia, sdLDL was found to be associated with an increased risk for CHD [22]. But the determination of plasma sdLDL levels was not widely used in clinical practice due to the disadvantages of being labour intensive, technically demanding, expensive, and slow to produce results. Thus, TG/HDL-C might be a surrogate marker for sdLDL with better clinical and economic significance. In a survival analysis in men, the TG/HDL-C ratio was significantly associated with CHD and all-cause mortality after adjustment for established risk factors [23]. In a retrospective study, da Luz et al. [24] found that a ratio of TG/HDL-C larger than four is the most powerful independent predictor for CHD development. However, the association of the TG/HDL-C ratio with CHD needs to be further studied [11].

The VLDL-C/HDL-C ratio was not associated with CHD in our study. Little data exist on the association between VLDL-C/HDL-C ratio and CHD. However, VLDL-C can reflect the plasma levels of atherogenic remnants (chylomicron remnants or IDL), which were highly correlated with CHD [25]. Hence, VLDL-C is a potential target of lowering plasma lipoprotein remnants.

In the present study, the CHD group had older age and higher male ratio than the control group (Table 1). Initially, an age and sex matched control group was intended to be formed, but we failed continuously after the subjects who did not fulfil the inclusion criteria were excluded. In order to rule out the possible effects of age and sex on the results, the effects of the lipoprotein ratios (TC/HDL-C, LDL-C/HDL-C, non-HDL-C/HDL-C, and apoB100/apoAI) on CHD risk were adjusted for a number of non-lipid variables, including age and sex, in the multivariate logistic regression analyses (Table 3), and the results (i.e. OR, 95% CI, and p value) before or after adjustment were not materially altered (Tables 2, 3). It is well known that atherogenic dyslipidaemia is frequently observed in diabetic patients, characterised by high TG concentration, low concentration of HDL-C, and the presence of sdLDL. Diabetes may have an effect on the results of the present study. Therefore, the associations between the lipoprotein ratios and CHD risk were also adjusted for diabetes in the multivariate logistic regression analyses, and the results were not significantly altered. Our data indicated that the ratios of TC/HDL-C, LDL-C/HDL-C, non-HDL-C/HDL-C, and apoB100/apoAI were independently associated with CHD after adjustment for non-lipid coronary risk factors.

### *Limitations of the study*

Our study has several limitations. First, the present study was not designed to examine all the risk factors associated with CHD. Rather, the specific goal was to examine whether the lipoprotein ratios were superior to conventional lipid parameters as predictors for CHD. Second, our study mainly focused on CHD patients whose lesions of the coronary artery were 50% or more in at least one major branch according to the diagnostic criteria. Those with mild coronary stenosis (less than 50%) were not categorised into the CHD group although they also had some risk of acute coronary syndrome. Thirdly, the patients were not from the general population but rather visitors to our hospital, which may have led to a selection bias.

## CONCLUSIONS

In conclusion, the results of this study suggest that the lipoprotein ratios are better predictors for CHD than conventional lipid parameters, and apoB100/apoAI could be the best predictor for CHD risk. Our data have added to the growing body of data suggesting that coronary risk assessment based exclusively on LDL-C is not optimal.

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### *References*

1. Yusuf S, Hawken S, Ounpuu S et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. Lancet, 2004; 364: 937–952.
2. Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. Circulation, 2002; 106: 3143–3421.
3. Stone NJ, Robinson JG, Lichtenstein AH et al. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation, 2014; 129: S1–45. doi: 10.1161/01.cir.0000437738.63853.7a.
4. Boekholdt SM, Arsenault BJ, Mora S et al. Association of LDL cholesterol, non-HDL cholesterol, and apolipoprotein B levels with risk of cardiovascular events among patients treated with statins: a meta-analysis. JAMA, 2012; 307: 1302–1309. doi: 10.1001/jama.2012.366.
5. Kinosian B, Glick H, Garland G. Cholesterol and coronary heart disease: predicting risks by levels and ratios. Ann Intern Med, 1994; 121: 641–647.
6. Hsia SH, Pan D, Berookim P, Lee ML. A population-based, cross-sectional comparison of lipid-related indexes for symptoms of atherosclerotic disease. Am J Cardiol, 2006; 98: 1047–1052.
7. Kastelein JJ, van der Steeg WA, Holme I et al. Lipids, apolipoproteins, and their ratios in relation to cardiovascular events with statin treatment. Circulation, 2008; 117: 3002–3009. doi: 10.1161/CIRCULATIONAHA.107.713438.
8. Millán J, Pintó X, Muñoz A et al. Lipoprotein ratios: Physiological significance and clinical usefulness in cardiovascular prevention. Vasc Health Risk Manag, 2009; 5: 757–765.
9. Goswami B, Rajappa M, Mallika V et al. Apo-B/apo-AI ratio: a better discriminator of coronary artery disease risk than other conventional lipid ratios in Indian patients with acute myocardial infarction. Acta Cardiol, 2008; 63: 749–755.

10. McQueen MJ, Hawken S, Wang X et al. Lipids, lipoproteins, and apolipoproteins as risk markers of myocardial infarction in 52 countries (the INTERHEART study): a case-control study. Lancet, 2008; 372: 224–233. doi: 10.1016/S0140-6736(08)61076-4.
11. Tamang HK, Timilsina U, Singh KP et al. Apo B/Apo A-I Ratio is Statistically A Better Predictor of Cardiovascular Disease (CVD) than Conventional Lipid Profile: A Study from Kathmandu Valley, Nepal. J Clin Diagn Res, 2014; 8: 34–36. doi: 10.7860/JCDR/2014/7588.4000.
12. Walldius G, Jungner I, Aastveit AH et al. The apoB/apoA-I ratio is better than the cholesterol ratios to estimate the balance between plasma proatherogenic and antiatherogenic lipoproteins and to predict coronary risk. Clin Chem Lab Med, 2004; 42: 1355–1363.
13. Pan L, Lu G, Chen Z. Combined use of apolipoprotein B/apolipoprotein A1 ratio and non-high-density lipoprotein cholesterol before routine clinical lipid measurement in predicting coronary heart disease. Coron Artery Dis, 2014; 25: 433–438. doi: 10.1097/MCA.0000000000000100.
14. Sniderman AD, Jungner I, Holme I et al. Errors that result from using the TC/HDL C ratio rather than the apoB/apoA-I ratio to identify the lipoprotein-related risk of vascular disease. J Intern Med, 2006; 259: 455–461.
15. Yang D, Liu X, Xiang M. The correlation between lipids ratio and degree of coronary artery stenosis. High Blood Press Cardiovasc Prev, 2011; 18: 53–56. doi: 10.2165/11593480-000000000-00000.
16. Genest J, McPherson R, Frohlich J et al. 2009 Canadian Cardiovascular Society/Canadian guidelines for the diagnosis and treatment of dyslipidemia and prevention of cardiovascular disease in the adult — 2009 recommendations. Can J Cardiol, 2009; 25: 567–579.
17. Manninen V, Tenkanen L, Koskinen P et al. Joint effects of serum triglyceride and LDL cholesterol and HDL cholesterol concentrations on coronary heart disease risk in the Helsinki Heart Study. Implications for treatment. Circulation, 1992; 85: 37–45.
18. Frost PH, Havel RJ. Rationale for use of non-high-density lipoprotein cholesterol rather than low-density lipoprotein cholesterol as a tool for lipoprotein cholesterol screening and assessment of risk and therapy. Am J Cardiol, 1998; 81: 26B–31B.
19. Sniderman AD, St-Pierre AC, Cantin B et al. Concordance/discordance between plasma apolipoprotein B levels and the cholesterol indexes of atherosclerotic risk. Am J Cardiol, 2003; 91: 1173–1177.
20. Rader DJ, Davidson MH, Caplan RJ, Pears JS. Lipid and apolipoprotein ratios: association with coronary artery disease and effects of rosuvastatin compared with atorvastatin, pravastatin, and simvastatin. Am J Cardiol, 2003; 91: 20C–23C.
21. Gaziano JM, Hennekens CH, O'Donnell CJ et al. Fasting triglycerides, high-density lipoprotein, and risk of myocardial infarction. Circulation, 1997; 96: 2520–2525.
22. Gardner CD, Fortmann SP, Krauss RM. Association of small low-density lipoprotein particles with the incidence of coronary artery disease in men and women. JAMA, 1996; 276: 875–881. doi: 10.1515/cclm-2014-0396.
23. Vega GL, Barlow CE, Grundy SM et al. Triglyceride-to-high-density-lipoprotein-cholesterol ratio is an index of heart disease mortality and of incidence of type 2 diabetes mellitus in men. J Investig Med, 2014; 62: 345–349. doi: 10.231/JIM.0000000000000044.
24. da Luz PL, Cesena FH, Favarato D, Cerqueira ES. Comparison of serum lipid values in patients with coronary artery disease at < 50, 50 to 59, 60 to 69, and > 70 years of age. Am J Cardiol, 2005; 96: 1640–1643.
25. Varbo A, Benn M, Tybjærg-Hansen A et al. Remnant cholesterol as a causal risk factor for ischemic heart disease. J Am Coll Cardiol, 2013; 61: 427–436. doi: 10.1016/j.jacc.2012.08.1026.


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# Współczynniki stężeń lipoprotein są lepszymi czynnikami predykcyjnymi choroby wieńcowej niż konwencjonalne parametry lipidowe w populacji osób należących do chińskiej grupy etnicznej Han

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## Streszczenie

**Wstęp i cel:** Dyslipidemia jest głównym czynnikiem ryzyka choroby wieńcowej (CHD). Pomiar stężenia lipidów w osoczu w Chinach standardowo stosuje się do prognozowania ryzyka, ale konieczne są dalsze badania, aby ocenić, czy współczynniki stężeń lipoprotein stanowią lepsze czynniki prognostyczne CHD niż konwencjonalne parametry lipidowe.

**Metody:** W populacji osób należących do chińskiej grupy etnicznej Han przeprowadzono badanie kliniczno-kontrolne w warunkach szpitalnych, obejmujące 738 chorych na CHD oraz grupę kontrolną liczącą 157 osób. Zebrano dane demograficzne oraz dotyczące stężeń lipidów i apolipoprotein w osoczu. Przeprowadzono jedno- i wieloczynnikową analizę regresji logistycznej w celu zbadania zależności między współczynnikami stężeń lipoprotein a ryzykiem CHD.

**Wyniki:** W grupie CHD następujące parametry miały istotnie wyższe wartości niż w grupie kontrolnej ($p < 0,05$ dla wszystkich): wiek badanych, stężenie frakcji cholesterolu innych niż HDL (non-HDL-C), stężenie lipoproteiny (a) [Lp(a)], współczynniki triglicerydy (TG)/HDL-C, cholesterol całkowity (TC)/HDL-C, lipoproteiny o małej gęstości (LDL-C)/HDL-C, non-HDL-C/HDL-C, lipoproteiny o bardzo małej gęstości (VLDL-C)/HDL-C i apolipoproteina B100/apolipoproteina AI (apoB100/apoAI). Ponadto w grupie chorych na CHD stwierdzono większy odsetek osób płci męskiej, palących tytoń i chorujących na nadciśnienie tętnicze. Wyniki jednoczynnikowej analizy regresji logistycznej wykazały, że współczynniki TC/HDL-C (iloraz szans [OR]: 1,135; 95% przedział ufności [CI] 1,019–1,265), LDL-C/HDL-C (OR 1,216; 95% CI 1,033–1,431), non-HDL-C/HDL-C (OR 1,135; 95% CI 1,019–1,265) i apoB100/apoAI (OR 1,966; 95% CI 1,013–3,817) istotnie zwiększają ryzyko wystąpienia CHD. Po przeprowadzeniu wieloczynnikowej analizy regresji logistycznej nie stwierdzono znaczącej zmiany wyników i każdy z czterech współczynników był niezależnie związany z CHD po skorygowaniu względem nielipidowych czynników ryzyka CHD. Współczynnik apoB100/apoAI najsilniej korelował z CHD, zarówno w analizie jednoczynnikowej, jak i wieloczynnikowej.

**Wnioski:** Dane uzyskane przez autorów wskazują, że współczynniki stężeń lipoprotein są lepszymi czynnikami predykcyjnymi CHD niż konwencjonalne parametry lipidowe. Spośród tych współczynników największą wartość w prognozowaniu ryzyka CHD ma stosunek stężeń apolipoprotein — apoB100/apoAI.

**Słowa kluczowe:** choroba wieńcowa, współczynnik stężeń lipoprotein, apoB100/apoAI, dyslipidemia, predyktor

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